REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested. Claims 21-32, 34-36, 38-43, 45-59, 61-63 and 65-71 are pending. No claims have been amended.

Rejections Under 35 U.S.C. 103(a)

Claims 21-27, 30-32, 34-36, 38-40, 42, 43, 45-54, 57-59, 61-63, 65-67 and 69-71 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal *et al.* (WO 96/18731, "Deggerdal") in view of Nargessi (U.S. Patent No. 6,855,499, "Nargessi").

Applicants respectfully traverse this ground of rejection. In the previous response, Applicants argued that Deggerdal teaches away from combining with Nargessi because Deggerdal teaches that increased viscosity (*e.g.*, from DNA contamination) is undesirable in RNA preparation, and the method of Nargessi requires adding polyalkylene glycol to the sample. In response to the above arguments, it is stated in the Office Action that

> "However, Deggerdal's statements regarding increased viscosity from DNA contamination relate to problems with sample handling in purified samples of RNA. By contrast, the method of Nargessi does not introduce polyalkylene glycol into the final purified sample, but rather uses it in the binding and wash buffers. These buffers are used only to load the sample onto the solid phase and wash the solid phase, and are not present in the final purified sample." (*see*, last paragraph on page 7 of the Office Action)

Applicants respectfully disagree with the above statements. Applicants submit that problems associated with increased viscosity from DNA contamination identified in Deggerdal are **not** limited to those with sample handling in purified samples of RNA. For example, Deggerdal provides "DNA increases viscosity making sample handling difficult leading to poor RNA yield and also RNA of poor quality with the likelihood of DNA contamination" (*see*, page 2, lines 1 to 4 of Deggerdal). One of ordinary skill in the art would interpret the problems associated with increased viscosity from DNA are due to the presence of DNA in the sample from which RNA is purified, which leads to poor RNA yield and quality. In other words, one skilled in the art would **not** read the above quoted sentence to indicate that

increased viscosity from DNA contamination only related to sample handling in purified samples of RNA. The above interpretation of one skilled in the art may find further support on page 14, lines 5-11 of Deggerdal. More specifically, Deggerdal provides that "[a] particularly advantageous embodiment of the invention is to use the isolation method of the invention to remove DNA from a sample prior to isolation of RNA, such that the viscosity of the lysed sample is reduced and a specific isolation of RNA molecule is favoured which again reduced or avoids the possibility for DNA contamination of RNA" (emphasis added).

Applicants further submit that Deggerdal teaches reducing viscosity resulting from not only the presence of DNA, but also the presence of chaotropic salt, during RNA purification. More specifically, in the first full paragraph on page 4, Deggerdal regards direct mRNA purification using guanidinium isothiocyanate (GTC) as disadvantageous because "the viscosity of cell lysates in 4M GTC is high and the beads are not effectively attracted by the magnet, resulting in an increased risk for DNA contamination, both for beads and other solid phases and lower yields." Moreover, when describing another method where nucleic acids are bound to silica particles in the presence of a chaotropic agent such as a guanidinium salt, Deggerdal regards the requirement for chaotropes at high molarity in this method as disadvantageous because chaotropes at high molarity result in viscous solutions that may be difficult to work with, especially in RNA work (*see*, second and third full paragraphs on page 4 of Deggerdal).

Applicants submit that the cited references, either alone or in combination, fail to teach or suggest the methods claimed in the present application. More specifically, there is no sufficient motivation for one of ordinary skill in the art to combine Deggerdal with Nargessi. Contrary to the assertion in the Office Action, Deggerdal itself in fact teaches away from being combined with Nargessi. Deggerdal teaches that, as discussed above, an agent that increases viscosity (*e.g.*, DNA and a chaotropic agent) should be avoided during cell lysis or the mixing of cell lysis with a solid phase in a RNA purification method. Nargessi is directed to a method for isolating nucleic acid using magnetic or paramagnetic particles encapsulated in a polymer such as cellulose or its derivatives (*see*, Abstract and column 1, lines 46-52). Such particles adsorb nucleic acids in the presence of a salt and polyalkylene glycol (preferably polyethylene glycol

with an average molecular weight of 8,000 (PEG 8000 MW)) at appropriate concentrations formulated as a binding buffer (column 4, lines 4 to 36). Because the binding of nucleic acid to the magnetic or paramagnetic particles requires the presence of both the salt and polyalkylene glycol in Nargessi, to modify Deggerdal in view of Nargessi, one has to add polyalkylene glycol to the lysing/binding buffer of Deggerdal. Because, as discussed above, Deggerdal teaches away from increasing the viscosity of the lysing/binding buffer and because including a polyalkylene glycol, such as 10% PEG 8000 MW used throughout the examples of Deggerdal, in the lysing/binding buffer would significantly increase the viscosity of the lysing/binding buffer, one of ordinary skill in the art would not have combined Deggerdal with Nargessi.

Claims 41 and 68 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal in view of Nargessi and further in view of the Calbiochem 2000-2001 reagent catalog.

Applicants respectfully traverse this ground of rejection. As discussed above, Deggerdal and Nargessi, either alone or in combination, fail to teach or suggest the method according to claim 21 or claim 45 of the present application to which claims 41 and 68 ultimately refer. Calbiochem 2000-2001 only relates to detergents and thus fails to remedy the deficiencies of Deggerdal and Nargessi.

Claims 28, 29, 55 and 56 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal in view of Nargessi and further in view of Heath *et al.* (WO 99/39009, "Heath").

Applicants respectfully traverse this ground of rejection. As discussed above, Deggerdal and Nargessi, either alone or in combination, fail to teach or suggest the method according to claim 21 or claim 45 of the present application to which the rejected claims directly or indirectly refer. Heath relates to DNA isolation and fails to remedy the deficiencies of Deggerdal and Nargessi.

In view of the above remarks, Applicants submit that the above grounds of rejection under 35 U.S.C. 103(a) have been overcome. Withdrawal of these rejections is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants believe that all of the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

/Qing Lin/

Qing Lin, Ph.D.
Registration No. 53,937

QXL:kw

701 Fifth Avenue, Suite 5400
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

1468658_1.DOC